Giving His All for ALL

A personal visit to Guatemala evolves into a sustained global outreach program in pediatric oncology.

In 2006, when Michael Dean, Ph.D., Head of CCR's Human Genetics Section of the Laboratory of Experimental Immunology, visited Guatemala as a volunteer member of his church, he never expected that the trip would be the first of many to the region, or that it would become the start of a global outreach program in pediatric oncology.

Dean's story began when he met a teacher on that first trip to the country, who told him about Edgar, a seven-year-old orphan who had what sounded like retinoblastoma, a rare type of eye cancer that usually develops in early childhood. Dean connected Edgar with the Unidad Nacional de Oncología Pediátrica in Guatemala City where they diagnosed a form of ocular herpes rather than the cancer feared by Dean.

That experience brought Dean in contact with both the pediatric oncology hospital in Guatemala and St. Jude Children's Research Hospital in Memphis, Tenn., two institutions that have been international partners to improve the lives of children since 1997.

The diverse genetic makeup of the Guatemalan people forms a complex backdrop for clinical oncology studies, and Dean wanted to investigate the role that this diversity plays in childhood cancers, especially the genetic risk factors for acute lymphoblastic leukemia (ALL), the leading cause of cancer-related deaths among children. Previous research had identified genetic variants (called polymorphisms) in the *ARID5B* gene, a gene implicated in early B-cell development, as possible culprits, showing also that certain variants are more prevalent in Hispanic children than in Caucasian children.

Conducting clinical research in a busy pediatric hospital in Central America, where staff handle ten times the number of cases seen in a typical U.S. pediatric center, was a huge challenge, and Dean faced it head on, personally taking each family through the consent process in Spanish. After Dean's team had collected more than 1,000 DNA samples, they confirmed that certain genetic polymorphisms at the ARID5B allele within the Guatemalan population confer much higher risks for ALL. In fact, when Dean's research team compared the frequency of the risk variants in three major populations, they showed that individuals of European descent had a 30 percent frequency, Hispanics had 50 to 60 percent, and the indigenous Mayan population had an even higher frequency of 70 percent.

Why is this particular genetic polymorphism so powerfully linked to ALL? One possible hypothesis is that many of today's indigenous Guatemalan people descended from individuals who survived infectious diseases brought to the Americas by Europeans. The surviving individuals may have had a stronger immune system due to the presence of the ARID5B allele, which resulted in a greater production of B cells to fight infections. That increased production of B cells could now be conferring a higher risk of ALL on the young descendants of these populations.

(Photo: J. Summers, SPCM, NCI-Frederick)

Michael Dean, Ph.D.

Knowing that certain variants of the *ARID5B* gene confer a high risk for ALL, particularly in Guatemalan children, may one day enable clinicians to customize cancer care by specifically targeting the protein products of these particular polymorphisms. But before that can happen, Dean and his team will continue this international collaboration to unravel the molecular role that these variants play in cancer.

To learn more about Dr. Dean's research, please visit his CCR Web site at http://ccr.cancer.gov/staff/staff.asp?Name=dean.